Breast Cancer Prophylaxis in BRCA+ Women

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Background & Purpose

Of the 1.6 million women diagnosed with breast cancer per year, many are caused by the inherited BRCA gene mutation.[1] Women who are BRCA positive have a 69-72% chance of developing breast cancer in their lifetime. For those who do develop breast cancer there is a 40% chance of a second recurrence in the contralateral breast within 20 years for BRCA1 and 26% in BRCA2.[2] The BRCA gene is easily recognized through genetic testing but the information given on prophylaxis to diagnosed women lacks the proper guidelines.

The goal of this research is to educate medical professionals on the correct medical practices in prophylaxis of breast cancer in women who have tested positive for the BRCA gene mutation. Patient's current options include observation with yearly screening, estrogen receptor modulator drugs like Tamoxifen, or bilateral risk reducing mastectomy. This review of studies aims to focus on which option, either Tamoxifen or BRRM, is the better choice for those with the BRCA gene mutation trying to avoid the development of breast cancer in the future.

PICOT

Does the pharmacotherapy Tamoxifen or Bilateral Risk-Reducing Mastectomy better prevent the incidence of breast cancer in women who've tested positive for the BRCA gene mutation?

Design & Methods

Keywords: BRCA gene mutation, tamoxifen, tamoxifen side effects, mastectomy, mastectomy complications, breast cancer prophylaxis

Inclusion: BRCA positive, female, no previous diagnosis of cancer, peer reviewed, full text available, and written in an English language

Exclusion: BRCA negative, currently going through chemotherapy, diagnosed with breast cancer, full text not available, and not written in English

Database	Yielded	Reviewed	Included in Analysis
Google Scholar	2,660	27	9

Synthesis of Evidence

After applying this criteria, nine studies were selected for review and analysis. Studies involve one longitudinal, one randomized double blind, two retrospective, one multicenter cohort, two meta-analysis, and two research surveys. The outcomes observed in the reviewed studies bring to light the most effective form of breast cancer prophylaxis for women with the BRCA gene mutation. Secondary endpoints of this review involve mortality rates associated with the choice of prophylaxis as well as reasoning from real patients on whether or not to proceed with certain forms of prophylaxis.

Results:

Prophylactic mastectomies are the most effective approach for reducing breast cancer with a proven 90% reduction of incidence after bilateral mastectomy with and without those with the BRCA gene mutation. No new breast cancers were observed after bilateral prophylactic mastectomy in any BRCA gene mutation carrier.[2]

In comparison, women with the BRCA gene mutation who took Tamoxifen had a 10.9% incidence of cancer in the follow-up period while those who did not take the drug had a 14.3% incidence of cancer development.[3]

A reviewed study observed 83% of BRCA1 breast cancers are ER negative while 76% of BRCA2 breast cancers are ER positive. Tamoxifen reduced breast cancer incidence by 62% among BRCA2 carriers due to their ER positive composition while not reducing the incidence of breast cancer in those with BRCA1 gene mutation due to it's ER negative composition.[4]

Type of Prophylaxis	Breast Cancer Incidence
Observation	14.3%
Tamoxifen	10.9%
BRRM	<0.13%

Abbreviation Key

BRRM: bilateral risk reducing mastectomy
BRCA: breast cancer gene

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Best Practice

Bilateral risk reducing mastectomy provides the most effective approach to decreasing the incidence of breast cancer in BRCA positive women.[2] Surgery is a permanent and life altering commitment that some women feel is to risky due to the procedures high complication rate, as well as feeling they will not be happy with the cosmetic outcome even though the complication rate is higher for those using the procedure as cancer treatment rather than prophylaxis.[5] Tamoxifen is much less efficacious as a whole in reducing cancer risk but does decrease the chance of cancer in those with BRCA2 mutation more than those with the BRCA1 mutation.[4]

Limitations

- Each of the studies involved in the review of breast cancer prophylaxis had a small number of participants and did not have a significant period of time for follow-up.
- Studying this topic is limited to the ethical problem of not being able to limit the choice of cancer prophylaxis to future patients, therefore limiting the ability for randomized controlled trials.
- In a study reviewed, participants were from the Netherlands where cancer prophylaxis is much more sensitive due to annual MRI's. Negative outcomes due to surgical complications might have been lessened compared to those in the US due to earlier detection of cancer.[6]
- Data in the reviewed studies were self reported and can yield errors.
- There were unforeseen factors in the decision making process of receiving a BRRM versus Tamoxifen. Some patients cannot be cleared for prophylactic surgery or may have other comorbidities that make contraindicate surgery, requiring the use of Tamoxifen instead.
- Comorbidities and QOL of patients was not reported. Lifestyle habits like diet and exercise were also not reported and can provide a source of risk reduction.[7]

Conclusion:

Overall BRRM is statistically the better option for breast cancer prophylaxis over Tamoxifen but decisions need to be made on a personal and multidisciplinary approach. Tamoxifen cannot be researched by controlled trials. The drug has many side effects yet BRRM involves major surgery that can possibly lead to complications and negative cosmetic outcomes. The question of the best approach cannot be fully answered due to patient autonomy to their own medical decision making involving their breast cancer prophylaxis.

References:

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